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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| EXAMINER | |
|---|---|
| ART UNIT | PAPER NUMBER |
| | 5 |

**DATE MAILED:**

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 09/340,595 | Applicant(s) PODHAJCER ET AL |
|---|---|---|
| | Examiner Thomas G. Larson, Ph.D | Art Unit 1635 |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,6-8,15-17,25,26 and 36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6-8,15-17,25,26 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12* .
4)☐ Interview Summary (PTO-413) Paper No(s) _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

1. The following action is responsive to Applicant's request for reconsideration in the paper filed 6/26/01.

2. As per applicant's request, the following clarification is made to the record. Claims 23-27 were inadvertently indicated as having been withdrawn from further consideration in the Office action mailed 12/27/00. Only claims 29-35 should have been indicated as having been withdrawn from further consideration.

3. Amended claim 6 is objected to because of the following informalities: Claim 6 is dependent from claim 5, but claim 5 was canceled in the amendment filed 6/26/01. To facilitate compact prosecution, claim 6 has been treated as depending from claim 1, since claim 5 ultimately depends from claim 1. Appropriate correction is required.

4. The rejection of claims 1, 6-8, 15-17, 25, 26, and 36 under 35 USC 112, 1st ¶, for lack of an adequate written description is withdrawn in view of applicant's amendments to the claims.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 25 and 26 stand rejected under 35 U.S.C. 102(b) as being anticipated by Everitt et al. (document no. AR2 on the PTO-1449 submitted with the information disclosure statement filed 10/28/99) for the reasons set forth in the Office action mailed 12/27/00.

Amended claims 25-26 are drawn to a plasmid or viral vector capable of transferring genetic material into a human cell encoding an antisense polynucleotide that which binds to and inhibits expression of human osteonectin mRNA.

Applicant's arguments filed 6/26/01 have been fully considered but they are not persuasive. Applicant traverses the rejection on the grounds that base claim 25 has been amended to recite a vector capable of transferring genetic material into a human cell and an antisense polynucleotide that which binds to and inhibits expression of human osteonectin mRNA.

In response to the argument that claim 25 now specifies a vector capable of transferring genetic material into a human cell, Everett et al. teach that the vectors constructed are eukaryotic expression vectors (p. 136, ¶ bridging cols. 1 and 2, especially lns. 1-4). Therefore, even though Everett et al. use these vectors to transfer genetic material into a murine cell line, they would be also be capable of

transferring genetic material into human cells since human cells, like murine cells, are eukaryotic cells.

In response to the argument that claim 25 now specifies an antisense polynucleotide that binds to and inhibits expression of human osteonectin mRNA, the fact that Everett et al. use the mouse ortholog of the human osteonectin transcript to construct the antisense sequence does not preclude it from binding to the human transcript. The osteonectin sequences appear to be highly related, as evidenced by the specification at p. 1, ¶ 2, lns. 7-9. Swaroop et al. (document designated AR11 on the PTO-1449 submitted with the information disclosure statement filed 10/28/99) indicate that the coding regions of the mouse and human osteonectin (SPARC) cDNA sequences share 85% sequence similarity (p. 41, ¶ bridging cols. 1 & 2). Given that Everett et al. use a 1.1 kb section of the mouse coding region in the antisense orientation to generate the osteonectin antisense polynucleotide (Everett, Fig. 1), it is likely that the antisense construct of Everett et al. would be capable of binding to and inhibiting expression of the human sequence if expressed in a human cell.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 6-8, 15-17, and 36 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons set forth in the Office action mailed 12/27/00.

Applicant's arguments filed 6/26/01 have been fully considered but they are not persuasive. Applicant traverses the rejection on the grounds that the art cited by the examiner as supporting a finding of lack of enablement for pharmaceutical compositions and therapeutic applications of antisense do not "...represent the present state of the art." However, it is submitted that it is the state of the art at the time the invention was made that must be considered (note MPEP 2164.05(a)), not the state of the art at the time of examination on the merits. It is submitted that Stull et al., Gewertz et al., Rojanasakul et al., Mercola et al., Orkin and Motulsky, and Crystal all summarize the state of the art at the time that the invention was made, as evidenced by the fact that they were published about the time of applicant's 1996 priority claim. Jen et al. was published after the filing date of the present application, but serves as evidence that many of the obstacles disclosed by the earlier publications still persisted at that date.

Applicant has made Lewis et al. of record as evidence that the skilled artisan would be able to successfully apply the invention in a therapeutic capacity at the time it was made. However, as specifically pointed out by applicant's response,

Lewis et al. state that their cytofectin "...offers the potential for use in *in vivo* applications ..." This statement, taken in proper context is understood to be a statement of potential, future application, not actual, present application. The teachings of Lewis et al. are all directed to application in cell culture, not therapeutic applications. Therefore, Lewis et al. is not seen as providing the necessary teachings required to allow the skilled artisan to routinely apply antisense oligonucleotides in a therapeutic capacity at the time the invention was made.

Applicant also makes US Patent No. 5,248,671 of record, stating that "issued patents are presumed valid under 35 USC 282." It is noted that every application is considered on its own merits, and that it is the issued claims of a US patent, not the disclosure as a whole, that is presumed valid under 35 USC 282. In the case of the '671 patent, the issued claims are drawn to methods of killing cancer cells using antisense oligonucleotides. Methods of therapy and pharmaceutical compositions are not claimed as they are in the instant application. Further, the specification of the '671 patent provides a working example of using antisense oligonucleotides to kill cancer cells cultured *in vitro* and *ex vivo* (Example 1).

With regard to the remaining patents cited by applicant, the claims of the 5,442,049 and 5,457,189 patents are drawn to antisense oligonucleotides, not to pharmaceutical compositions or to methods of therapy. The remaining patents were all issued after applicant's priority date and, therefore, do not provide evidence of

what was publicly available to the skilled artisan at the time the instant invention was made.

9. No claim is allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The OFFICIAL FAX numbers are (703) 308-4242 and (703) 308-3014. The faxing of such papers must conform with the notices published

in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Unofficial papers, such as draft responses and proposed amendments, may be transmitted directly to the examiner's computer at (703) 746-7019. If an official paper is to be faxed to this number, it is recommended that the examiner be notified before doing so.

Any inquiry concerning this communication or earlier communications should be directed to Thom Larson, whose telephone number is (703) 308-7309. The examiner normally can be reached Monday through Friday from 9:00 AM to 5:30 PM, EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Receptionist, whose telephone number is (703) 308-0196.

Thomas G. Larson, Ph.D.
Examiner